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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/121,798	07/23/1998	ROBERT BRIDENBAUGH	018484-00120	3701

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Peter K. Seperack
Townsend and Townsend and Crew LLP
Two Embarcadero Center, 8th Floor
San Francisco, CA 94111-3834

EXAMINER	
VOGEL, NANCY S	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/121,798	BRIDENBAUGH ET AL.	
	Examiner	Art Unit	
	Nancy Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/29/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 23-43 are pending. Receipt of the amendment filed 8/29/03 is acknowledged.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/29/03 has been entered.

Specification

The amendment filed 8/29/03 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: paragraph [0010], page 3, line 10 of the specification; paragraph [0033], page 7, line 27; paragraph [0034], page 8 line 1; paragraph [0040], page 9, line 26; paragraph [0064], page 19, line 1; paragraph [0083] page 24, line 5; paragraph [0085] page 24, lines 17, 18, 20.

Applicant is required to cancel the new matter in the reply to this Office Action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23-43 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-62 of U.S. Patent No. 6,011,148 in view of Nochumson et al. (US Pat. Appl. Publ. No. US2001/034435 A1) (cited by applicants).

Claims 1-62 of US Pat. No. 6,011,148 recite a method of preparing purified plasmid DNA comprising a) circulating the solution through an open channel ultrafiltration unit for sufficient time to allow a gel layer to form; b) filtering the solution through the ultrafiltration unit collecting the retentate solution, filtering the solution through a 0.2 um filter, applying the purified plasmid DNA to a positively charge ion exchange chromatography resin wherein the plasmid DNA is eluted from the resin with a gradient. The claims recite that the solution comprising the plasmid DNA is obtained from the lysis of bacterial cells using a detergent containing buffer and the substantial

removal of cellular debris and proteins. The methods of the claims differ from claims 23- 43 in that they fail to disclose that the positively charged ion exchange chromatography resin is a trimethylamino ethyl (TMAE) anion exchange chromatography resin, alkaline lysis is utilized, and static mixers are utilized. However, the portion of US Pat No. 6,011,148 that teaches ion exchange resin teaches that many different positively charged resins may be used, and the portion that discloses lysis of cells discloses that any known conventional procedure for lysis may be used (col. 5, lines 49-55). Nochumson et al. discloses that TMAE anion exchange resin may be used in a method of purification of plasmid DNA (see col. 8, lines 34-46), and alkaline lysis of cells (see abstract). Wan et al. disclose a method of plasmid purification in which lysis is by alkaline solution, and static mixers are used. It would have been obvious to modify the method of claims 1-62 of US Pat. No. 6,011,148 such that alkaline lysis was used to lyse cells, and TMAE anion exchange resin was used in the anion exchange chromatography step and static mixers are used, in view of the disclosure by Wan et al. and Nochumson et al. of the usefulness of these steps in purification of plasmids. One having ordinary skill in the art would have been motivated to make such a modification to obtain better purification of plasmid DNA through the use of a well known, commercially available anion exchange resin useful for DNA purification, the well known alkaline lysis technique, and static mixers, as disclosed by Nochumson et al. and Wan et al.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 23-26, 29 are rejected under 35 U.S.C. 102(e) as being anticipated by Nochumson et al. (US Pat. Appl. Publ. No. US2001/0034435 A1) (cited by applicants).

Nochumson et al. disclose a method for purifying plasmid DNA comprising: a) contacting a solution comprising plasmid DNA with a trimethylamino ethyl (TMAE) anion exchange chromatography resin, the solution having a conductivity at which the plasmid DNA is bound to the resin; b) washing the resin to elute endotoxin; and c) eluting the plasmid DNA with a step or continuous gradient of increasing conductivity (see page 4, para [0041] – [0045], Fig. 3, page 6, paragraphs [0074]-[0080], claims 18-27.)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 37-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Nochumson et al. (US Pat. Appl. No. US 2001/0034435 A1), in view of Wan et al. (US Pat. No. 5,837,529) Lee et al. (US Pat. No. 6,197,553), Lee et al. (US Pat. No. 6,197,553), and Song et al. (J. Chem. Soc. Faraday Trans. 1995, 91(19), 3389-3398) (all of record).

Nochumson et al. disclose a method for purifying plasmid DNA comprising: a) lysing cells with alkaline conditions, b) removal of precipitated proteins, chromosomal DNA and cell debris (paragraphs 0049, 0074-0075), c) filtration (paragraph 0076), d) contacting a solution comprising plasmid DNA with a trimethylamino ethyl (TMAE) anion exchange chromatography resin, the solution having a conductivity at which the plasmid DNA is bound to the resin e) washing the resin and f) eluting the plasmid DNA with a step or continuous gradient of increasing conductivity (paragraph 0077) g) ultrafiltration/diafiltration followed by sterile filtration (paragraph 0079) (see page 4, paragraphs 0041 – 0045, Fig. 3, page 6, paragraphs 0074-0080, claims 18-27.). The

reference discloses that the lysis solution and precipitation/neutralization solution is mixed with the cells by flowing through in-line static mixers (paragraph 0084).

The difference between the reference and the claims is that the reference does not disclose the use of at least one glass fiber filter and at least one nylon filter prior to anion exchange chromatography, RNAse is not used, and the step of purifying used ultrafiltration in the presence of a gel layer is not specified.

However, Lee et al. disclose a method of plasmid purification in which RNAse is used to eliminate RNA prior to filtration and anion exchange purification (paragraph bridging col. 2-3). Two filtration steps of the lysate are disclosed (col. 7, lines 5-10). Wan et al. disclose a method for purifying large quantities of plasmid DNA for pharmaceutical use by mixing a solution of bacterial cells comprising plasmid DNA with an alkaline lysis solution by flowing through a first static mixer to obtain a lysate, and contacting the lysate with a precipitating solution by flowing through a second static mixer, thereby forming a precipitation mixture (see abstract, figures, and col. 2-4). The precipitation solution is potassium acetate (col. 4, line 23-24), and the lysing solution is alkaline (col. 4, lines 17-19). Wan et al. disclose filtering the lysate through membrane filter to remove insoluble materials, and subjecting the filtrate to ultrafiltration to remove impurities (see col. 1, lines 42-54). The reference discloses that the material of the membrane filter may be any commercially available filter, preferably with a pore size of 0/1-0.2 um. (col. 2, lines 38-46). Song et al. disclose that the process of ultrafiltration involves the development of a polarization layer of the solute on the ultrafiltration membrane, which provides a resistance to flow through the ultra filter. The presence of

this layer provides a gel layer through which all other solute must pass (see page 3390, col. 2, Figs. 1 and 2, and page 3394, col. 1, and discussion at page 3396, col. 2) .

It would have been obvious to one of ordinary skill in the art at the time of filing of the instant application to combine the method for purifying plasmid DNA from such impurities as endotoxin, with the steps from methods for purifying plasmid DNA disclosed by Wan et al. and Lee et al., because they were all involved in the process of purifying large quantities of plasmid DNA for pharmaceutical use. One would have been motivated to do so by the disclosed advantages of such steps as RNAse treatment (removal of RNA molecules, an impurity), filtration (removal of debris impurities), and ultrafiltration (removal of impurities). Song et al. provides the theoretical background teaching that a gel layer would be present in an ultrafiltration process.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ntv

JAMES KETTER
PRIMARY EXAMINER